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Electron rich salen-AlCl catalysts as efficient initiators for the ring-opening polymerisation of *rac*-lactide

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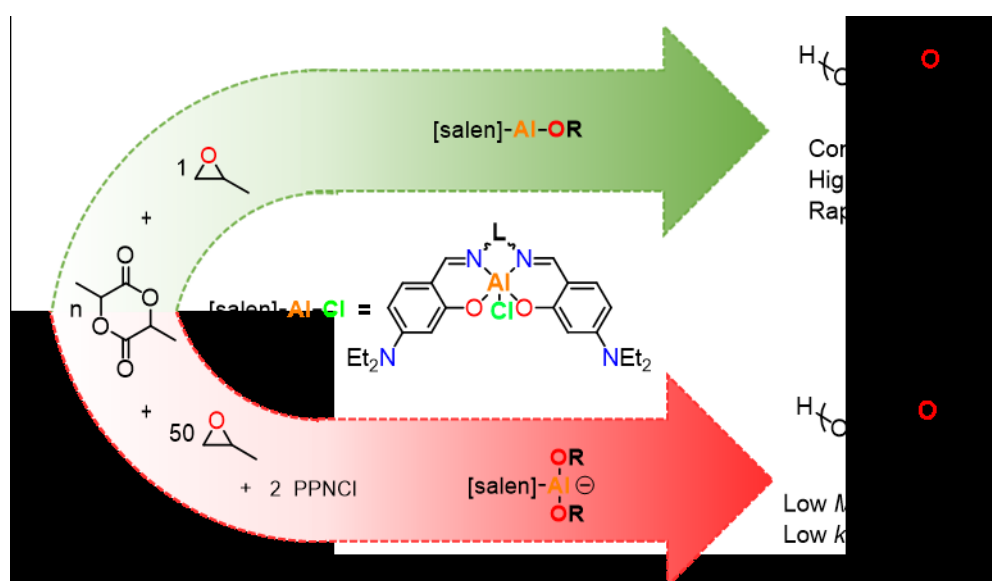
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Abstract

The ring-opening polymerisation of lactide is a useful means to prepare biodegradable materials with well controlled polymer architectures and bespoke material properties. While homogeneous ligand-Al-OR complexes have shown great success in this field, initiation from ligand-AlCl complexes has lagged behind. Here, we report four new salen-AlCl complexes featuring NEt₂-substituents, which display high catalyst activities towards *rac*-lactide ring-opening polymerisation ($k_{\text{obs}} < 1.9 \times 10^{-3} \text{ s}^{-1}$) *via in situ* activation with a single equivalent of propylene oxide. Incorporating Lewis basic NEt₂ groups into the ligand scaffold not only improves the initiation efficiency but also avoids the need for a Lewis basic co-catalyst and excess epoxide. Notably, studies of our amino-substituted catalysts reveal that the formation of a hexacoordinate aluminate species may hinder rather than enhance catalytic activity.

Graphical Abstract



Introduction

Aliphatic polyesters are essential as biodegradable materials with a broad range of applications including packaging,[1, 2] electronics[3] and medical devices.[4, 5] In particular, poly(lactic acid) (PLA) has many commercial applications due to its physical and mechanical properties. Ring-opening polymerisation (ROP) is one of the most efficient routes to prepare PLA with targeted material properties, which is achieved through careful control of the polymer microstructure. Some of the most powerful catalyst systems are homogeneous organometallic complexes, and aluminium-salen catalysts have garnered particular focus thanks to high catalyst activities, the low toxicity of the metal and a high level of control over the polymer microstructure.[6, 7]

Most of the highly effective aluminium catalysts for *rac*-lactide (*rac*-LA) ROP feature alkoxide initiating groups. However, recent studies by Thomas, Maron *et al.* revealed that salen-AlCl catalysts, which are generally poor initiators for ROP,[8] could achieve high catalyst activities when combined with an epoxide and an onium salt co-catalyst to generate an Al-alkoxide *in situ* (Figure 1).[9] This method of initiating ROP and ring-opening copolymerisations has gathered attention,[10-12] and epoxides have been utilised as *in situ* activators for *rac*-LA ROP with porphyrin-AlCl,[13] Sn(octanoate)₂,[14] and salen-FeCl systems.[15-17] The homogeneous Al-Cl catalysts generally require the presence of a co-catalyst such as PPNCl for efficient ROP initiation. These onium salts are proposed to enhance initiation through Lewis base coordination to the metal centre (Figure 1, Step A), increasing the nucleophilicity of the metal-chloride bond towards epoxide ring-opening. This Lewis base coordination is also proposed to enhance the nucleophilicity of the metal-alkoxide bond towards the ring-opening of *rac*-LA, facilitating propagation.[9] The interaction between the catalyst and the co-catalyst is likely to occur through a reversible equilibrium (Step A), with the pentacoordinate Al complex providing a vacant site for epoxide coordination and activation towards nucleophilic attack (Figure 1, Step B). On the basis of detailed mechanistic studies using a salen-AlCl/propylene oxide (PO)/PPNCl catalyst system based on the Jacobsen ligand, Thomas, Maron *et al.* proposed that initiation occurs through the formation of a highly nucleophilic hexacoordinate aluminate complex (Figure 1, Step C).[9] Notably, neutral aluminium chloride and aluminium alkoxide complexes were suggested to be inactive under the conditions investigated. The experimental set-up therefore involved overnight reaction of the Jacobsen-AlCl catalyst with PPNCl in PO solvent, to form the active initiator species prior to the addition of *rac*-LA. These insightful studies highlighted the ability of salen-AlCl species to efficiently polymerise *rac*-LA at ambient temperature. However, translation of this system to an industrial set-up may be limited by the need for excess epoxide (PO is highly toxic), an expensive PPNCl co-catalyst, and an overnight pre-activation of the catalyst components prior to the addition of *rac*-LA. Modification of the ligand scaffold offers the potential to alter the electronics at the metal centre and therefore influence the initiation mechanism and propagation rate.

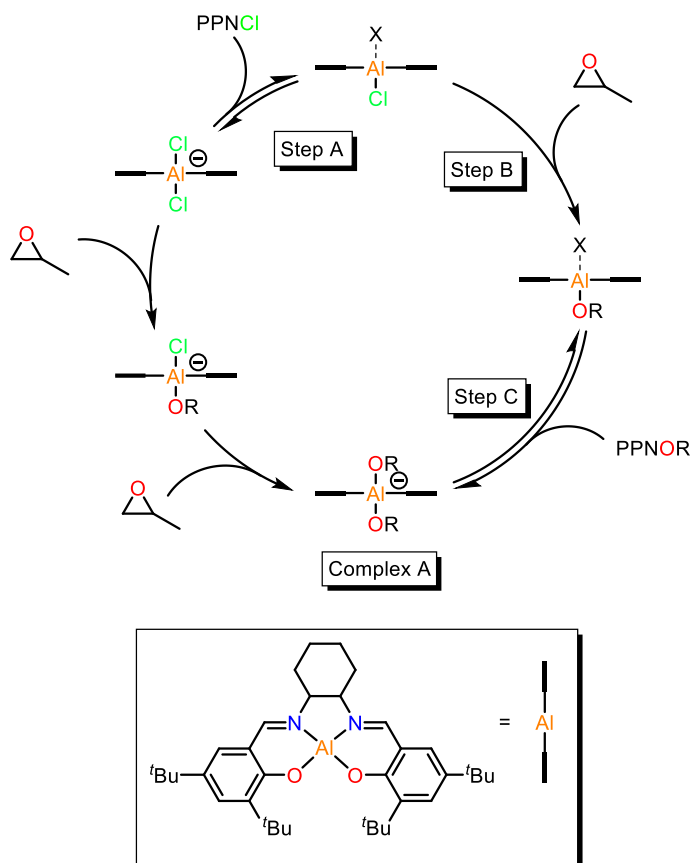
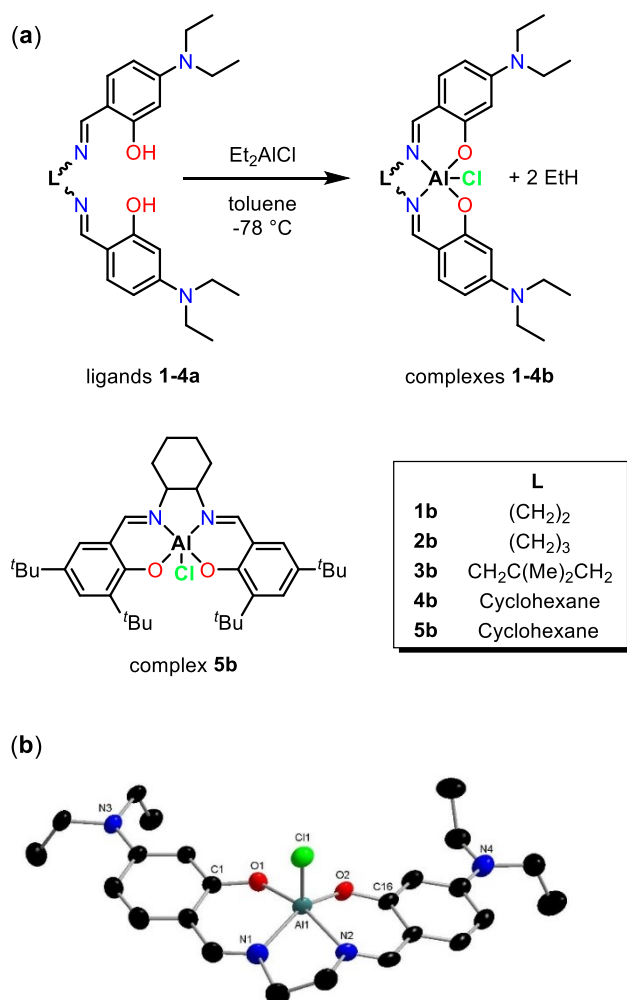


Figure 1 Suggested activation mechanism using a salen-AlCl complex. For the aluminate species, the cationic PPN⁺ moiety has been omitted for clarity and X denotes a vacant site for epoxide coordination.[9]

This work explores the synthesis of a series of four salen-AlCl complexes bearing diethylamino substituents on the phenolic rings. The choice of this strongly electron donating substituent was driven by the desire to reduce the initiation period observed when using salen-AlCl complexes with epoxides as *in situ* activators. We hypothesized that strongly electron donating amine substituents would increase the nucleophilicity of the Al-chloride by stabilising the formation of a partial cationic charge on Al upon dissociation of the chloride group. Furthermore, we hoped that the electron donating effect may overcome the requirement for a Lewis base onium co-catalyst (Figure 1, Step A and/or Step C), avoiding the formation of a hexacoordinate Al species and opening up additional sites for monomer coordination. Here we show these complexes are able to overcome some of the current limitations observed with other salen-AlCl catalysts for the ROP of *rac*-LA.

Results and Discussion

A series of salen-AlCl complexes was synthesised by a straightforward two-step procedure (Scheme S1). *Meta*-diethylamino salicylaldehyde was selected due to the strongly electron donating amine groups *para*- to the imine group (Scheme 1a), enabling delocalisation of the lone pair of electrons to the imine nitrogen. To understand the impact of this ligand modification upon the Al-Cl bond strength, complex **1b** was recrystallised from hot THF, affording yellow needle crystals. Single crystal X-ray diffraction studies revealed that the aluminium centre is penta-coordinate, connected to two phenolic oxygens, one chloride and two datively coordinated imine nitrogens (Scheme 1b). While the Al-N and the Al-O bond lengths are in the expected range for aluminium salen complexes, the Al-Cl bond is relatively long [Al1-Cl1, 2.200(2) Å] (Table S1).[18-24] The extended length and therefore lability of the Al-Cl bond are likely to result from the electron-donating diethylamino substituents increasing the electron density at the Al centre hence increasing the polarisation of the Al-Cl bond. Salen-AlCl complexes may offer some advantages in stability and ease of handling compared to salen-Al-alkyl catalysts (Figure S14).[25]



Scheme 1 (a) Synthesis of salen-AlCl complexes (**1b-4b**) and structure of salen-AlCl complexes **1b-5b** (refer to Scheme S1 for reagents and conditions). (b) Molecular structure of **1b** with displacement ellipsoids at the 50% probability level. THF solvent and hydrogen atoms have been omitted for clarity. Only one of two independent molecules in the unit cell is displayed (Figure S15).

Complexes **1b**, **2b**, **3b** and **4b** were tested for *rac*-LA ROP in the presence of PO (Table 1) using toluene solvent at 120 °C with a catalyst:PO:*rac*-LA ratio of 1:50:100. Under these conditions, all four complexes displayed catalytic activity towards *rac*-LA ROP (Table 1). As a control reaction, complex **1b** was tested in the absence of PO showing that both components are required for polymerisation. While the comparison of catalysts **1-4b** against other salen-Al systems is difficult, due to the range of conditions used, all four complexes demonstrate relatively high catalyst activities (Figure 2, Table S3-S4). Complexes **2b** and **3b**, bearing more flexible propyl diamine backbones, displayed significantly higher catalytic activities (**2b**, $k_{\text{obs}} = 1.1 \times 10^{-3} \text{ s}^{-1}$; **3b**, $k_{\text{obs}} = 1.2 \times 10^{-3} \text{ s}^{-1}$) than complexes **1b** ($k_{\text{obs}} = 7 \times 10^{-5} \text{ s}^{-1}$) and **4b** ($k_{\text{obs}} = 8 \times 10^{-5} \text{ s}^{-1}$). This observation falls in line with reported trends for related salen-AlCl complexes,[26-28] where increased activities have been attributed to the greater flexibility of the linking unit and distortion toward a trigonal bipyramidal geometry.[26] These conformational changes have been proposed to increase the accessibility of key transition states involved in the ROP process. The polymerisation kinetics showed a first-order dependence in monomer concentration, in line with typical ROP of lactide proceeding via a coordination-insertion mechanism.[29-32] All four complexes show a similar isotactic bias (Table 1), with P_i values ranging from 0.69 (**4b**) to 0.74 (**2b**). While many studies have investigated the effect of steric bulk of *ortho*-substituents upon tacticity through a chain end control mechanism, the significance of *meta*-substituents is less well known. These findings suggest that bulky *meta*-substituents may allow some control over the inverse relationship between the rate of polymerisation and the degree of isotacticity.

The molecular masses determined by GPC analysis ($M_{n,\text{obs}}$) generally gave good agreement with the theoretical values ($M_{n,\text{calc}}$), indicating a well-controlled polymerisation (Table 1). However the dispersity broadened at high conversions (>85%, Table S4), suggesting that chain transfer and/or transesterification may predominate in the late stages of the ROP (Table S4),[33] as has been observed for related catalyst systems.[9, 29, 34] MALDI-ToF analysis confirmed that the polymerisation could be initiated by the Al-chloride group ring-opening PO, as a series of α -chloropropoxyl, ω -hydroxyl end-capped PLA was observed (Figure S18). In addition, a second series corresponding to initiation by propylene diol was observed. Propylene diol is known to be present as an impurity in CO₂/epoxide ring-opening copolymerisation (typically formed from the *in situ* reaction of PO with trace water, Figure S20 and S21),[35] and has been shown to act as a mono- or bi-functional chain transfer agent (CTA).[36] Unfortunately, MALDI-ToF analysis could not discern whether each propylene diol initiated one or two propagating chains due to the identical mass (HOCH₂CH₂(CH₃)O and H end groups for monofunctional chain transfer vs internal OCH₂CH₂(CH₃)O and two H end groups for bifunctional chain transfer). However, it is possible that bifunctional chain transfer contributes towards the broad dispersities observed at high conversions, as the rate of chain transfer with the (less reactive) secondary alcohol unit may become competitive with propagation at high conversions. Some cyclic PLA was also observed at low molecular weights.

Table 1 Ring-opening polymerisation of *rac*-LA mediated by catalysts **1b-4b**^[a]

Entry	Catalyst	Time (min)	% Conversion ^[b]	$M_{n,calc}$ / Da ^[c]	$M_{n,obs}$ / Da ^[d]	\bar{D} ^[d]	P_i ^[e]
1	1b	40	19	2726	-	-	-
2	1b	120	43	6184	3150	1.2	0.70
3	2b	20	70	10140	8650	1.2	0.71
4	2b	40	90	13010	13270	1.7	0.74
5	3b	20	72	10319	7780	1.3	0.70
6	3b	40	94	13543	7840	2.0	0.70
7	4b	40	13	1920	-	-	-
8	4b	120	39	5623	6030	1.1	0.69

[a] Reaction conditions: [catalyst]/[PO]/[*rac*-LA] = 1:50:100, [*rac*-LA] = 1 M in toluene, 120 °C. [b] Determined by ¹H NMR spectroscopy. [c] Calculated as ([*rac*-LA]/[catalyst])×(%conversion/100)×MW of lactide. [d] Determined by gel-permeation chromatography (GPC) in THF solvent, universal calibration relative to polystyrene standards, M_n was calculated considering Mark–Houwink’s corrections for M_n ($M_n(calc) = 0.58[M_n(GPC)]$).[34] [e] P_i values determined through ¹H{¹H} NMR spectroscopic analysis using the method proposed by Coates and Oviatt.[37]

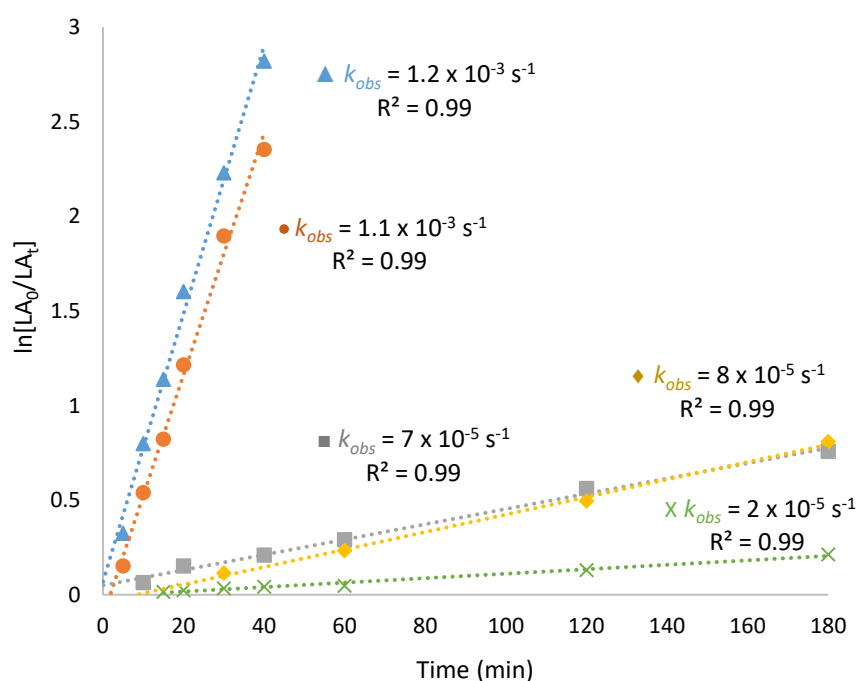


Figure 2 Kinetic plot of $\ln[LA]_0/\ln[LA]_t$ versus time for the ROP of *rac*-LA catalysed by complexes **1b** ■, **2b** ●, **3b** ▲, **4b** ◆, and **5b** X. Reaction conditions: [catalyst]/[PO]/[*rac*-LA] = 1:50:100, [*rac*-LA] = 1 M in toluene, 120 °C.

Kinetic studies of catalysts **1-4b** revealed a rapid initiation for all four complexes (Figure 2). This is particularly significant considering that closely related Jacobsen salen-AlCl complex **5b** (Figure 2) was reported to require pre-activation by stirring the catalyst, epoxide and co-catalyst (e.g. PPNCl) for 16

hours prior to reaction with *rac*-LA, albeit under different reaction conditions.[9] For comparison, **5b** was also tested in *rac*-LA ROP at 120 °C in toluene solvent (Figure 2). Highlighting the improved initiation using the diethylamino substituted salen ligand, **4b** displayed a reduced induction period (approximately 3.5 minutes) in comparison to the analogous Jacobsen complex **5b** (> 10 minutes). Furthermore, the induction period was significantly lower with complexes **1b-3b**, which is likely to arise from the greater flexibility of the diamine backbone. These findings suggest that the diethylamino substituents labilise the Al-Cl bond, in line with the molecular structure of **1b** (*vide supra*). Notably, Jacobsen complex **5b** also displays a significantly lower propagation rate than analogous **4b** (**4b**, $k_{\text{obs}} = 8 \times 10^{-5} \text{ s}^{-1}$; **5b**, $k_{\text{obs}} = 2 \times 10^{-5} \text{ s}^{-1}$). It may be expected that the electron donating amine substituents would decrease the Lewis acidity of the Al centre disfavours lactide coordination and insertion, yet the relative propagation rates of **4b** and **5b** suggest that this is not the case. The higher catalytic activity of **4b** may be due to the reduced steric bulk of the substituents facilitating lactide coordination, or possibly from a mechanistic difference between **4b** and **5b**.

To probe the initiation mechanism, the reaction between complex **1b** and PO in *d*₈-toluene was monitored by ¹H NMR spectroscopy (Figure S22). At ambient temperature, ring-opening of the epoxide was complete after 1 hour; it would be expected to occur much faster under the polymerisation conditions (120 °C). By comparison, the reaction between **5b** and PO was slower, taking 5 hours to reach completion (Figure S23). The ring-opening of PO can occur through nucleophilic attack at either the methylene carbon or the methine carbon (Figure S24); these competitive pathways have both been reported in literature.[38] However, NMR studies of complex **1b** and PO revealed that nucleophilic attack occurred exclusively at the methylene carbon (Figure S25).

Quaternary ammonium salts have been reported to enhance the catalytic activity of a variety of homogeneous Al-Cl catalysts[10, 13, 39] including **5b**. [9] However, addition of PPNCI (2 equivalents) to complex **2b** unexpectedly resulted in a 15-fold drop in reactivity (Figure 3). To eliminate the possibility of the reduced activity of **2b** arising from the interaction of PPNCI with the amine substituents, control reactions were performed in the presence of triethylamine (2 equivalents) (Table S6), which did not alter the catalyst activity. In contrast, the addition of 2 equivalents of PPNCI to catalyst **5b** (toluene solvent, 120 °C) increased the catalyst activity and gave non-linear kinetics (Figure S26). These observations suggest that the mechanism may be different for AlCl complexes based on the diethylamino substituted and the Jacobsen salen ligands (**1b-4b** vs **5b**).

Detailed experimental and computational studies by Thomas, Maron *et al.* suggest that in the presence of PO and PPNCI, Jacobsen catalyst **5b** initiates *rac*-LA ROP through the formation of a highly nucleophilic (bis)alkoxide “ate” type complex (Figure 1, complex **A**). [9] Under the reaction conditions investigated by Thomas, Maron *et al.* (room temperature, neat PO), all three components of the catalyst system (**5b**, PPNCI and PO) were essential for polymerisation to occur. To investigate potential mechanistic differences between **2b** and **5b**, diethylamino substituted **2b** was tested under these alternative conditions, and displayed significantly lower activity than **5b** (Figures S26 and S27). Contrary to the reaction in toluene, the catalytic activity of complex **2b** was enhanced by the addition of PPNCI in PO solvent. In spite of the enhanced activity, GPC analysis revealed a bimodal polymer distribution and poorer control over the polymer molecular weight with **2b**, suggesting that PPNCI

reduces the polymerisation control. Furthermore, kinetic analysis did not show the expected first-order dependence on monomer concentration (Figure 1, Figure S27). On the basis of these observations and previous literature reports,[9] it is plausible that there are two competing mechanisms operating under these conditions; firstly a mechanism which does not involve PPNCI (forming higher molecular weight polymers) and secondly, the formation of an “ate” complex (resulting in an induction period and lower molecular weight polymers). In contrast, catalyst **5b** gives a monomodal distribution but very low M_n values. Furthermore, a colour change from yellow to white was observed upon reaction of **2b** with PPNCI and PO, providing support for the formation of an “ate” complex.[10]

As the addition of PPNCI decreased rather than enhanced the activity of catalyst **2b** in toluene at 120 °C, there may be a different mechanism in operation between **2b** and **5b** under these conditions. While there is strong evidence for the formation of a highly reactive “ate” complex with **5b**,[9] the formation of an “ate” complex may hinder rather than enhance the reactivity of **2b** under certain reaction conditions. Although salen-Al “ate” complexes are difficult to determine experimentally,[9, 10] complex **1b** and PPNCI were combined in a 1:1 ratio in d_8 -THF solvent and analysed by ^1H NMR spectroscopy. The formation of an “ate” complex remained inconclusive, as the ^1H NMR spectra were indistinguishable aside from a minor shift of the amine backbone proton signals (Figure S29). This suggests that the reduced catalyst activity does not arise from an interaction between the co-catalyst and the amine substituents, as the NEt_2 proton resonances were identical in the presence and absence of PPNCI. Notably, a more significant shift was observed when complex **5b** was combined with PPNCI in d_8 -THF, although the nature of this interaction remains unclear (Figure S30).

For the Jacobsen system, the presence of a strong Lewis base (the chloride/alkoxide counterion of PPNX) has been reported to datively coordinate to Al to activate an Al-Cl/Al-O bond towards nucleophilic attack (Scheme 1, Step A and Step C). This process may account for the induction period observed with **5b** (Figure S28). For electron rich, diethylamino-substituted **2b**, the more labile Al-Cl bond may be activated simply by the presence of the epoxide, a weaker Lewis base. For catalyst **2b**, the presence of the stronger Lewis donor alkoxide/chloride (from PPNX) may block epoxide coordination hence reduce epoxide activation towards nucleophilic attack. To understand whether epoxide coordination to **2b** was essential to labilise the Al-Cl bond, catalyst **2b** was tested in the presence of just one equivalent of epoxide (Table S8). Catalyst **2b** displayed a slightly improved catalytic activity (1 equiv. PO, $k_{\text{obs}} = 1.9 \times 10^{-3} \text{ s}^{-1}$; 50 equiv. PO, $k_{\text{obs}} = 1.1 \times 10^{-3} \text{ s}^{-1}$) and a short induction period of approximately 3 minutes (Figure S32). The improved catalytic activity may arise from the lack of epoxide competing with lactide monomers for coordination at the metal centre. The $M_{n,\text{obs}}$ values were slightly higher than the $M_{n,\text{calc}}$ values, yet the chain length increased with conversion and the dispersities were narrow (Table S8). In contrast, 1 equivalent of PO resulted in reduced activity for **5b** (1 equiv. PO, $k_{\text{obs}} = 9 \times 10^{-6} \text{ s}^{-1}$; 50 equiv. PO, $k_{\text{obs}} = 2 \times 10^{-5} \text{ s}^{-1}$) (Figure S33). Furthermore, the addition of PPNCI to **5b** with one equivalent of PO prevented polymerisation rather than promoting it, indicating that excess PO is required. This dependence may arise because the active bis-alkoxide “ate” species (Figure 1, complex A) cannot be formed with just one equivalent of PO, excess epoxide may be required to promote epoxide coordination (hence activation towards ring-opening), and/or the polar PO solvent may be required to stabilise key “ate” intermediates. The ability to initiate with just

one equivalent of epoxide is of key importance, as this overcomes the need for an excess of the highly toxic epoxide, which, together with eliminating the need for a co-catalyst, brings significant environmental benefits.

To further investigate the influence of PPNCI in our reaction systems, catalyst **2b** was tested in the presence of varying equivalents of PPNCI (0.5 to 10 equivalents PPNCI vs **2b**, Table 2). Rather than a simple inhibition, PPNCI initially inhibits the polymerisation (0.5 to 5 equivalents) but on increasing the PPNCI:catalyst ratio (10 equivalents) then promotes polymerisation (Figure S34). To understand whether this activity decrease was related to a prolonged initiation period, rather than a decreased propagation rate, the reaction kinetics were analysed using 0.5, 1 and 2 equivalents of PPNCI vs catalyst (Figure S35). The polymerisation rate was significantly slower in the presence of PPNCI and the kinetics deviated slightly from the previously observed first order dependence in monomer (Figure 3: no PPNCI, $k_{obs} = 1.1 \times 10^{-3} \text{ s}^{-1}$; 2 equivalents, $8 \times 10^{-5} \text{ s}^{-1}$). Although the reactivity enhancement with 10 equivalents of PPNCI is not yet well understood, excess PPNCI may activate *rac*-LA (or the epoxide) toward ring opening. Indicative of an interaction between *rac*-LA and PPNCI, lactide improves the solubility of PPNCI in PO solvent and ^1H NMR spectroscopic analysis revealed a significant shift of the methine proton resonance when lactide was analysed in the absence ($\delta = 5.03$) or presence ($\delta = 5.07$) of PPNCI (Figure S36).

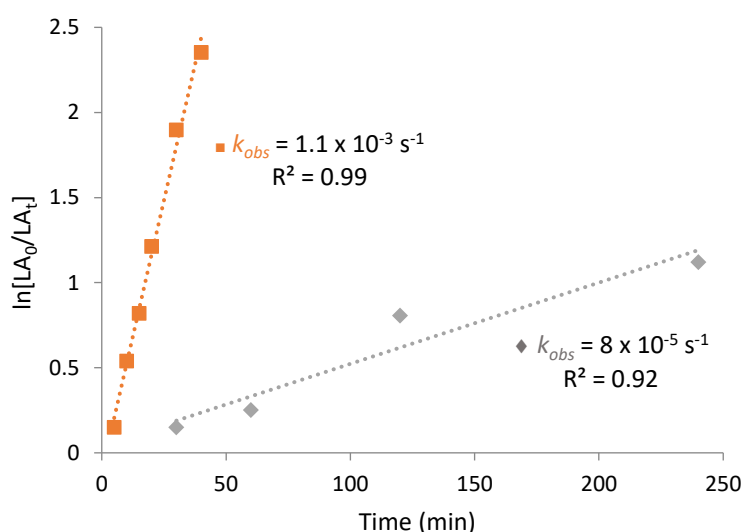


Figure 3 Kinetic plot of $\ln[\text{LA}]_0/\ln[\text{LA}]_t$ versus time for the ROP of *rac*-LA catalysed by complex **2b** with (♦) and without (■) 2 equivalents of PPNCI co-catalyst. Reaction conditions: $[\text{catalyst}]/[\text{PPNCI}]/[\text{PO}]/[\text{rac-LA}] = 1:2:50:100$, $[\text{rac-LA}] = 1 \text{ M}$ in toluene, 120°C .

Increasing the ratio of PPNCI:catalyst significantly reduced the polymer chain length ($M_{n,obs}/M_{n,calc}$ Table 2), suggesting that PPNCI can provide a nucleophilic chloride source to attack and ring-open an Al-coordinated epoxide. Towards the later stages of the polymerisation, bimodal distributions were observed, suggesting that the reaction is less well controlled in the presence of PPNCI (Table 2, entry 4; Figure S19). Notably, no conversion was observed in control reactions with only PPNCI, confirming that the salen-AlCl catalyst is required for activity, presumably through Lewis activation of the epoxide and lactide.[12] To test this hypothesis, alternative ammonium salts tetrabutylammonium bromide

(TBABr) and tetrabutylammonium iodide (TBAI) were investigated using catalysts **2b** and **5b** yielding similar reaction conversions to PPNCl (Table 2). Furthermore, chain end analysis by MALDI-ToF spectrometry revealed PLA terminated with a hydroxyl- and a bromo- or iodo-propoxyl group. While these observations suggest that the co-catalyst anion can initiate the polymerisation, halogen exchange between the aluminium chloride and the co-catalyst anion may also occur. Alternatively, the co-catalyst may act as a chain transfer agent (CTA, Figure 4). CTAs are typically protic sources such as mono- or bi-functional alcohols, which temporarily cap a propagating polymer chain and initiate a new chain under immortal polymerisation conditions thus reducing the polymer chain length (Figures S20 and S21, Table S5).[40] The decreased M_n values may arise from PPNCl acting as a CTA,[13, 39] exchanging the chloride anion with an aluminium-alkoxide group (where the alkoxide may either be the propagating polymer chain or the ring-opened epoxide) (Figure 4).

Table 2 Ring-opening polymerisation of lactide mediated by catalyst **2b** in conjunction with a quaternary ammonium salt co-catalyst after 30 minutes.^[a]

Entry	Co-catalyst	Co-catalyst equivalents	% Conversion ^[b]	$M_{n,calc}$ / Da ^[c]	$M_{n,obs}$ / Da ^[d]	$\bar{D}^{[d]}$	$M_{n,calc} / M_{n,obs}$
1	PPNCl	0	85	12241	13820	1.4	0.89
2	PPNCl	0.5	15	2157	-	-	-
3	PPNCl	1	12	1791	615	1.2	2.91
4	PPNCl	2	18	2585	520	1.2	4.97
5	PPNCl	5	50	5865	555	1.3	10.57
6	PPNCl	10	99	14202	835	1.4	17.01
7	TBABr	2	20	2818	585	1.3	4.82
8	TBAI	2	16	2286	620	1.2	3.69

[a] Reaction conditions: [catalyst]/[PO]/[rac-LA]/[co-catalyst] = 1:50:100:n, [rac-LA] = 1 M in toluene, 120 °C. [b] Determined by ¹H NMR spectroscopy. [c] Calculated as ([rac-LA]/[catalyst])×(%conversion/100)×MW of lactide, assuming that only one chain grows per catalyst system. [d] Determined by gel-permeation chromatography (GPC) in THF, universal calibration relative to polystyrene standard, M_n was calculated considering Mark-Houwink's corrections for M_n ($M_n(calc) = 0.58[M_n(GPC)]$).[34]

Previous reports proposed that with excess PO, catalyst **5b** undergoes an equilibrium between a salen-aluminium alkoxide/PPN alkoxide and a hexacoordinate (bis)alkoxide aluminium species (Figure 1, Step C).[9, 41-44] This could be viewed as a mode of chain transfer, through exchange of the propagating Al-alkoxide polymer chain for a dormant PPN-alkoxide chain (Figure 4). It seems plausible that this exchange could occur through the formation of a hexacoordinate anionic “ate” complex.[45, 46] Although there is limited literature evidence for the formation of such an “ate” complex,[47] Thomas, Maron *et al.*, investigated the catalyst activity of the alkoxide analogue of **5b**, salen-AlOⁱPr, with PPNCl, and observed PLA chains capped by both OⁱPr and Cl-propoxy groups.[9] Notably, increasing the number of PPNCl equivalents decreased the $M_{n,obs}$ value in line with each Cl initiating a polymer chain, which was proposed to occur through an “ate” mechanism. With our systems, in the presence of PPNCl, it remains unclear whether the secondary initiation comes from the ammonium salt acting as a CTA, exchanging the Cl and alkoxide ligands (Figure 4), or whether the ammonium salt anion can attack and open a coordinated epoxide (via the formation of an “ate” complex).

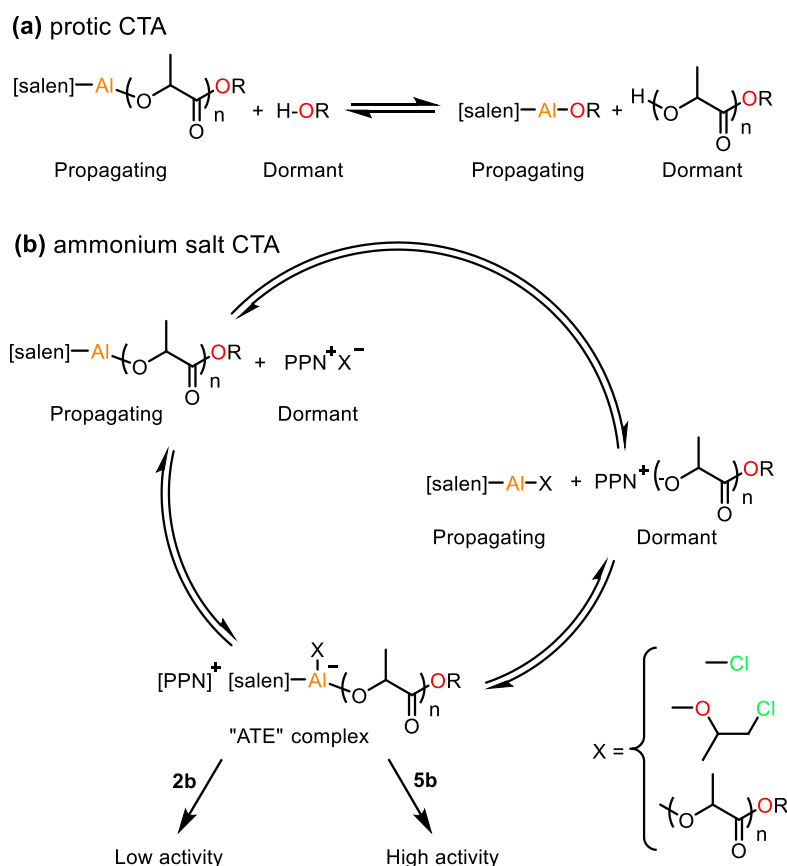


Figure 4 Proposed role of (a) protic chain transfer agents in *rac*-LA ROP; (b) ammonium salt chain transfer agents in *rac*-LA ROP (toluene solvent, 120 °C).

On the basis of our experimental observations, we propose the following mechanism for *rac*-LA ROP using **2b** and PPNCl (Figure 5). Firstly, the Al-Cl can attack a coordinated epoxide to form an Al-alkoxide species, which can then polymerise *rac*-LA. Alternatively, the Al-alkoxide group may be exchanged for an Al-Cl group through metathesis with PPNCl. The presence of additional equivalents of PPNCl may therefore disfavour the formation of the active Al-OR species by reforming the Al-Cl species and delaying propagation. MALDI-ToF spectroscopic analysis hints that this exchange may occur, as using TBABr or TBAI as the co-catalysts generated bromo- or iodo-propoxy end groups in addition to the chloro-propoxy end groups. Furthermore, PPNOR may play a role as a CTA, accounting for the reduced $M_{n,obs}$ values observed using a greater number of equivalents. This proposed chain transfer mechanism was probed via investigation of the quaternary ammonium alkoxide salt TBA-OMe. Intriguingly, catalyst **2b** with TBA-OMe polymerised *rac*-lactide, even in the absence of PO. Control polymerisations using only TBA-OMe (without catalyst **2b**) gave only trace conversion of *rac*-LA (<3% after 2 hours). This observation indicates that OMe/Cl ion exchange could occur (possibly via an "ate" complex), resulting in the formation of an active alkoxide catalyst species capable of producing isotactic PLA, albeit with a loss of control ($P_i = 0.70$, 57% conversion after 1.5 hours). It is a significant advantage that our catalyst system displays rapid initiation and efficient polymerisation in the absence of an expensive onium salt co-catalyst and with just one equivalent of epoxide. These observations are attributed to the presence of the electron donating diethylamino group labilising the Al-Cl bond towards epoxide attack and opening, and altering the Lewis acidity of the Al centre.

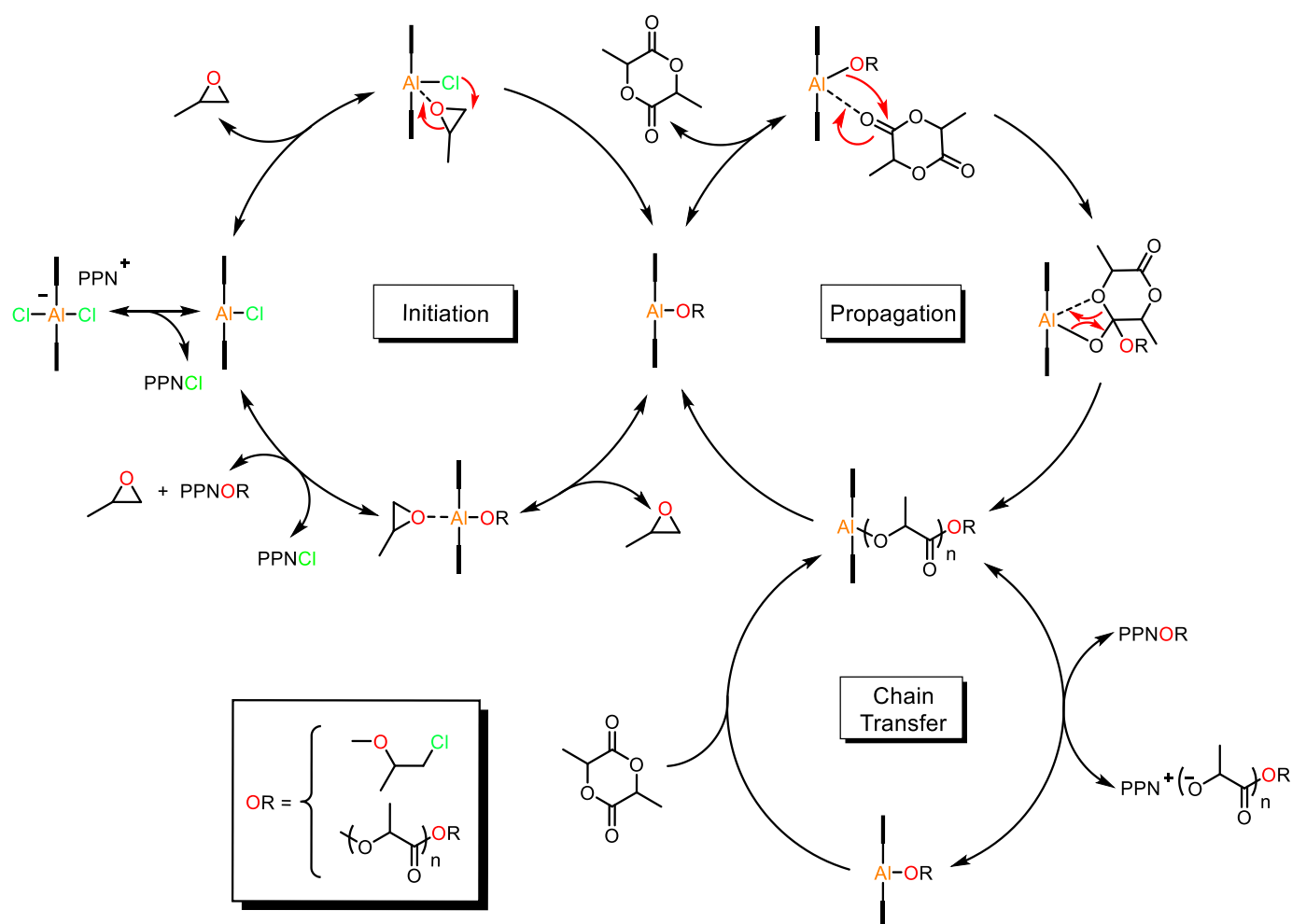


Figure 5 Proposed mechanistic pathway for *rac*-lactide polymerisation using catalysts **1b-4b**, PPNCl and PO.

Conclusions

In conclusion, a series of salen-AlCl complexes bearing *meta*-NEt₂ phenol substituents (**1b-4b**) were developed for the ROP of *rac*-LA. The new complexes were characterised through a combination of NMR spectroscopy, elemental analysis, mass spectrometry and X-ray crystallography. In the presence of propylene oxide, all four complexes display high catalyst activities and good control over the polymerisation. X-ray diffraction and NMR reactivity studies confirmed that the incorporation of electron donating amino substituents labilises the Al-Cl bond, which improves the initiation efficiency in comparison to the analogous Jacobsen salen-AlCl complex (**5b**). The increased Al-chloride reactivity avoids the need for a Lewis basic ammonium salt co-catalyst and the use of excess epoxide, which is highly toxic. Importantly, these factors bring benefits in terms of safety, cost and environmental impact. In toluene solvent, the addition of a PPNCl co-catalyst diminishes the activity of **1b-4b** but enhances the activity of **5b**, suggesting that the initiation mechanisms differ between the diethylamino-substituted ligands and the Jacobsen analogue. Overall, these results demonstrate the potential of salen-AlCl complexes bearing intramolecular Lewis bases as relevant alternatives for *rac*-LA ROP.

Conflicts of Interest

There are no conflicts of interest to declare.

Acknowledgements

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